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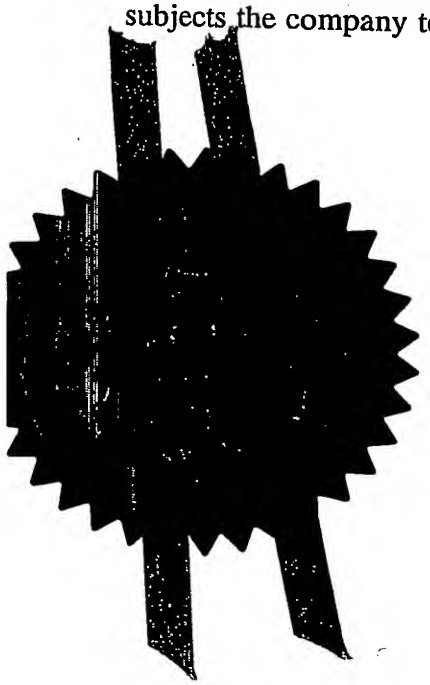

Signed

Dated 12 August 2003

GB 0218675.7

By virtue of a direction given under Section 30 of the Patents Act 1977, the application is proceeding in the name of

JOHNSON MATTHEY PLC,
2-4 Cockspur Street,
Trafalgar Square,
LONDON,
SW1Y 5BQ,
United Kingdom

Incorporated in the United Kingdom

[ADP No. 08519803001]

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The Patent Office

Cardiff Road
Newport
Gwent NP9 1RH

1	Your reference	SYN 51068
2	Patent application number *(The Patent Office will fill in this part)*	0218675.7 — 12 AUG 2002
3	Full name, address and postcode of the or of each applicant (underline all surnames)	IMPERIAL CHEMICAL INDUSTRIES PLC 20 Manchester Square, London, W1U 3AN
	Patents ADP Number *(if you know it)*	935003 — 935006
	If the applicant is a corporate body, give the country/state of its incorporation	United Kingdom
4	Title of the invention	Nitrogen-containing ligands
5	Name of Your Agent *(if you have one)*	GIBSON, Sara Hillary Margaret
	"Address for service" in the United Kingdom to which all correspondence should be sent *(including the postcode)*	Synetix Intellectual Property Department PO Box 1, Room N101 Belasis Avenue Billingham Cleveland England, TS23 1LB
	Patents ADP Number *(if you know it)*	7912484004

SECTION 20 (1977 ACT) APPLICATION FILED 9/12/02

6	If you are declaring priority from one or more earlier patent applications, give the country and the date of filing of the or each of these earlier applications and *(if you know it)* the or each application number	Country	Priority Application number *(if you know it)*	Date of Filing *(day / month / year)*

7	If this application is divided or otherwise derived from an earlier UK application, give the number and filing date of the earlier application	Number of earlier application	Date of Filing *(day / month / year)*

8	Is a statement of inventorship and of right to grant of a patent required in support of this request?	Yes

Answer yes if:
a) any applicant named in part 3 is not an inventor, or
b) there is an inventor who is not named as an applicant, or
c) any named applicant is a corporate body.
See Note (d)

Patents Form 1/77

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Continuation sheets of this form	-
Description	22
Claim(s)	3
Abstract	1
Drawings	-

10 If you are also filing any of the following state how many against each item

Priority documents	
Translations of priority documents	
Statement of Invention and right to grant of a patent *(Patents Form 7/77)*	
Request for Preliminary Examination and search *(Patents Form 9/77)*	
Request for Substantive Examination *(Patents Form 10/77)*	
Any other documents *(Please specify)*	

11 I/We request the grant of a patent on the basis of this application

Signature [signature] Date 12.8.2002

12 Name and daytime telephone number of person to contact in the United Kingdom

Sara H.M. Gibson
01642 522650

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Nitrogen-containing ligands

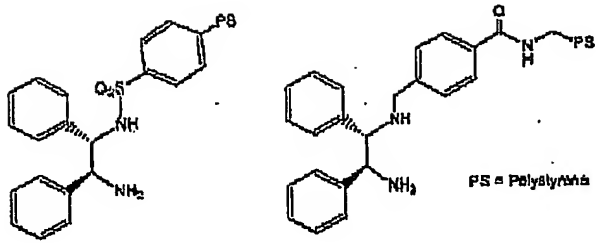
This invention relates to nitrogen-containing ligands and in particular to nitrogen-containing ligands supported on polymers, metal oxides or silica materials that provide a means for immobilising metal catalysts. Such immobilised metal catalysts are useful for accelerating and directing chemical reactions whose products are useful, for example, as chemical intermediates or reagents for use in the production of fine chemicals or pharmaceutical intermediates.

Nitrogen-containing ligands are a particularly useful group of ligands which find widespread use in asymmetric catalysis (see "*Nitrogen-containing ligands for asymmetric homogeneous and heterogeneous catalysis*", Fache et al, *Chem. Rev.*, 2000, 100, 2159-2231).

The fixing of homogeneous catalysts to solid supports provides the potential for extending the benefits of heterogeneous catalysts to homogeneous systems. These benefits include easier separation of catalyst and reaction products leading to shorter work up times and improved process efficiency, the potential for re-activation and re-use of the supported catalysts which are often based on expensive metals and complex ligand geometry, and the possible adaptation of the immobilised catalyst to continuous flow fixed-bed processes.

Strategies for homogeneous catalyst immobilisation have been based on absorption, ion exchange or tethering the catalysts to a support using covalent attachment. By covalent attachment we mean the formation of a covalent bond between support and catalyst. Covalent attachment is attractive for providing catalysts that may be more robust to catalyst leaching and hence retain higher activities upon re-use. Covalent attachment of the metal catalyst may be achieved by forming chemical bonds between a ligand and particles of a polymer, for example polystyrene, or oxide material, for example silica, that has been subjected to a surface functionalisation

Immobilisation of nitrogen-containing ligands, such as diamines to polymer supports is known, but attempts at covalent immobilisation of such ligands has been restricted to formation of bonds via functional groups linked to the nitrogen atom(s) of the ligands. For example the amine group may be reacted with a benzenesulphonyl-functionalised polymer (see Lemaire et al, *Synlett.*, 1997, 1257 and Williams et al, *Tetrahedron Lett.*, 2001, 42, 4037) or alternatively the amine group may be reacted with chlorosulphonylbenzoic acid and the resulting functionalised diamine reacted with aminomethylated polystyrene. (see Bayston et al, *Tetrahedron. Asymm.*, 1998, 9, 2015). These 'nitrogen- immobilised' diamines are depicted below.



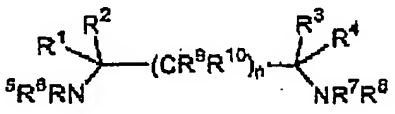
These catalysts however do not provide high levels of activity or selectivity, particularly upon re-use. For example, the ruthenium-catalysed reduction of acetophenone using the latter ligand was examined and the activity of the catalyst was found to decline markedly upon reuse and be dependent on the type of polymer used. It therefore appears that the immobilisation of nitrogen-containing ligands via the nitrogen atom(s) is undesirable because the presence of the linking groups on the nitrogen atoms effects the stability, activity and/or the selectivity of the catalysts.

Furthermore, the presence of a linking group attached to the nitrogen atom(s) of such nitrogen-containing ligands prevents useful derivatives such as Schiff bases or cationic ligands from being readily prepared.

We have found that immobilisation of the nitrogen-containing ligands may advantageously be performed via functional groups attached to carbon atoms linking the nitrogen atoms.

It has been proposed in our co-pending PCT application GB02/00527 to prepare an immobilised ligand by reaction of a functional group-containing ligand with an organofunctional silica, wherein the organofunctional silica is prepared by co-hydrolysis of an alkyl silicate and an organofunctional silane. That application specifically discloses immobilised phosphine ligands. While the aforementioned PCT application also suggested that nitrogen containing ligands such as diamines and Schiff bases could be employed as a functional group-containing ligands, it did not specifically disclose such ligands having functional groups attached to the carbon atoms linking the nitrogen atoms.

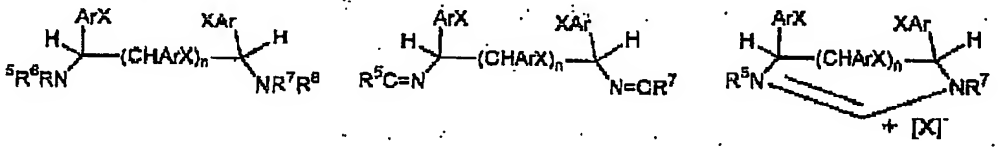
Accordingly the present invention provides an immobilised nitrogen-containing ligand comprising the reaction product of a compound of formula (I)



(I)

wherein R^5, R^6, R^7 and R^8 are independently hydrogen, a saturated or unsaturated C1-C10 alkyl group, an aryl group, a urethane group, a sulphonyl group or form an imine group, R^1, R^2, R^3 ,R^4, R^9 and R^{10} are independently hydrogen, a saturated or unsaturated C1-C10 alkyl group or an aryl group, n is 0-2, and at least one of R^1, R^2, R^3 ,R^4, R^9 and R^{10} is functionalised with a functional group, and a solid support having a site capable of reacting with said functional group.

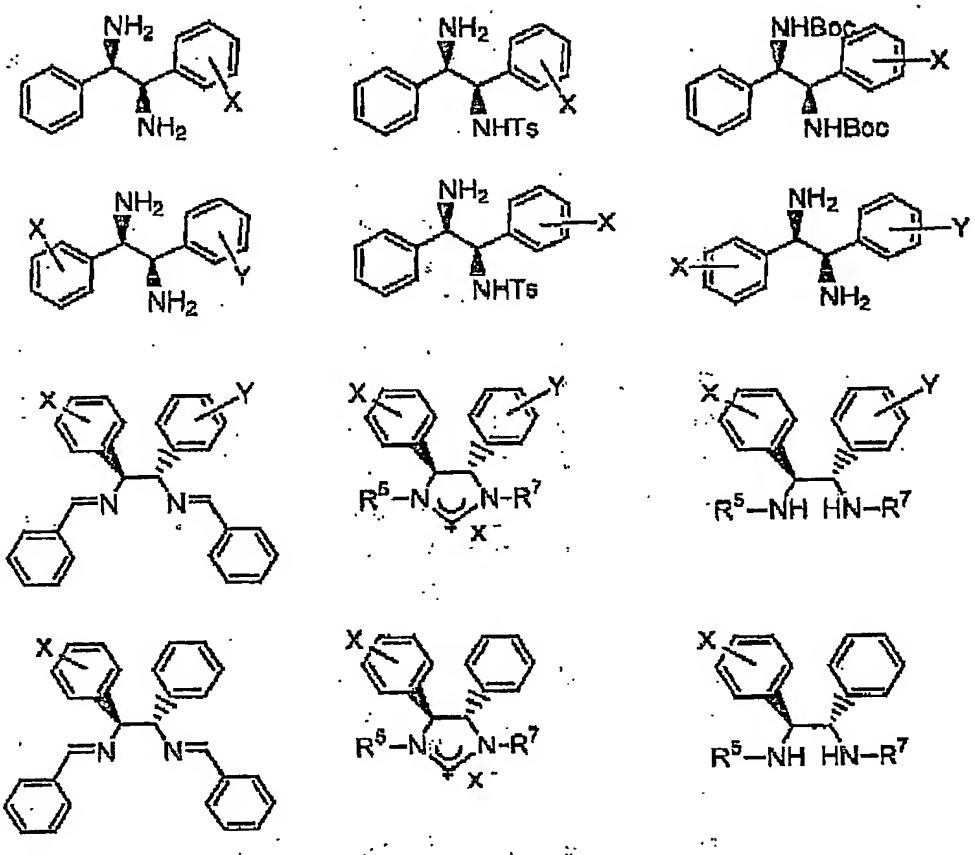
Preferably n is 0 or 1, R^1, R^3 and R^9 are hydrogen and at least one of R^2, R^4, and R^{10} is a functional group-containing aryl group. Where R^5, R^6, R^7 and R^8 are saturated or unsaturated C1-C10 alkyl groups or aryl groups, it will be understood that these groups may themselves further comprise functional groups selected from the list comprising halogen (Cl, Br, F or I), hydroxyl, carbonyl, carboxyl, nitrile, mercapto, alkoxy, amine, imine, amide and imide. Thus, in one embodiment the nitrogen containing ligand is a diamine where preferably, R^5, R^6, R^7 and R^8 are hydrogen, sulphonyl or urethane groups. In a further embodiment, NR^5R^6 and NR^7R^8 form imine (N=C) groups whereby R^6 and R^8 are omitted and R^5 and R^7 are as defined above, and in yet a further embodiment R^5 and R^6 form a ring linked by between 1 and 3 carbon atoms and R^5 and R^7 are as defined above. Examples of these embodiments, where n is 0 or 1, R^1, R^3 and R^9 are hydrogen and R^2, R^4, and R^{10} are functional group-containing aryl groups are depicted below;



Preferably R^1, R^2, R^3, R4, R^9 and R^{10} are chosen such that the nitrogen atoms are bonded to chiral centres and the nitrogen-containing ligand is chiral. The ligand may be homochiral, i.e. (R,R) or (S,S) or have one (R) and one (S) centre. Preferably the ligand is homochiral.

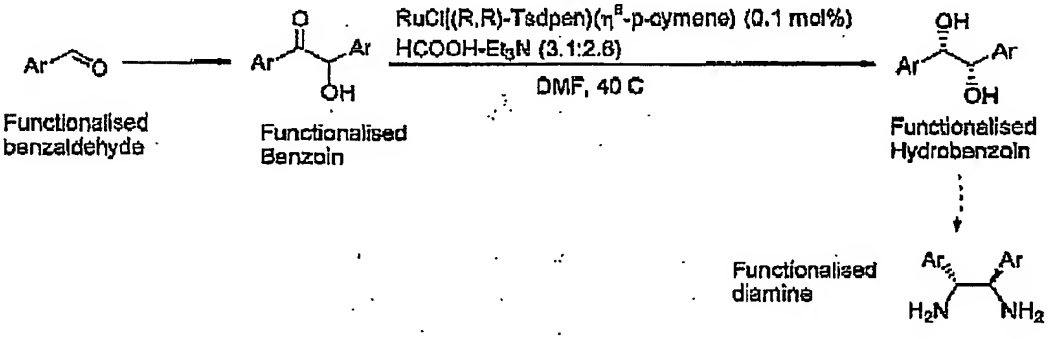
The functional group on at least one of R^1, R^2, R^3, R4, R^9 and R^{10} that may be used to bond to the support may be any that is capable of reacting with the support material and which does not prevent the catalytically active metal complex from reacting with the ligand. One or more functional groups may be present which may be the same or different. Such groups include halogen (Cl, Br, F or I), hydroxyl, alkoxy, carbonyl, carboxyl, anhydride, carbene, methacryl, epoxide, vinyl, nitrile, mercapto, amine, imine, amide and imide. The functional groups to be reacted with the solid support may conveniently be introduced into the nitrogen containing ligand during its preparation.

Suitable nitrogen containing ligands include but are not restricted to the following where X and Y are functional groups as defined above

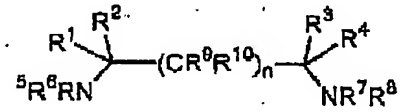


If a functional group available on the nitrogen-containing ligand is unsuitable for reaction with the solid support, it may be converted by chemical reaction or alternatively, the ligand may be reacted with a linker molecule that provides a suitable functional group capable of reaction with the solid support. The linker molecule may be any that contains a functional group that is capable of reacting with at least one of R^1, R^2, R^3, R^4, R^9 and R^{10} and provides a suitable functional group in the resultant ligand capable of reacting with the solid support. Suitable linker molecules include C1-C10 alkyl, alkoxy, e.g. polyethyleneglycol (PEG), alkyl-aryl, aryl, phenoxy or anilide compounds containing functional groups selected from halide, hydroxyl, carbonyl, carboxyl, anhydride, carbene, methacryl, epoxide, vinyl, nitrile, mercapto, isocyanate, amine, imine, amide and imide. In one embodiment the linker molecule is polyethylene glycol and preferably the linker molecule is PEG 2000 (i.e. a PEG having a molecular weight of about 2000). Advantages of preparing the nitrogen-containing ligand in this way are that new functional groups may be introduced in a way that is not generally possible in commercially available starting materials and that functional groups may be introduced at a greater distance from the nitrogen atom.

Methods for preparing enantiomerically pure 1,2- and 1,3-nitrogen containing ligands such as diamines, either directly by asymmetric synthesis or by synthesis of racemic mixtures followed by chiral resolution are known. We have found however that many of the routes to non-functionalised ligands do not work well for functionalised ligands. We therefore have developed a new route to preparing functionalised ligands, particularly 1,2-diamines and their derivatives such as Schiff bases or cationic compounds, based upon one used to prepare enantiomerically pure substituted hydrobenzoins, (see Noyori et al, *Org. Lett.* 1999, 1, 1119). Whereas in the presence of 0.1 mol% of RuCl[(R,R)-Tsdpen)(η^6-p-cymene), using a mixture of HCOOH-Et_3N (3.1:2.6) as hydrogen source, asymmetric transfer hydrogenation of benzils affords the (S,S)-hydrobenzoins quantitatively with high diastereomeric (>95% de) and enantiomeric purities (>99% ee), we have found that under the same conditions, replacement of the benzils with functionalised benzoins gives functionalised (S,S)-hydrobenzoins with same yield, de and ee, in which the benzoin with a chirally labile stereogenic center is converted to one major stereoisomer, (S,S)-product, via dynamic kinetic resolution. As functionalised benzoins can be readily prepared from the corresponding functionalised benzaldehydes by benzoin condensation, this route provides an efficient method to prepare enantiomerically pure functionalised 1,2-diarylethylenediamines. This route is depicted below;



Thus the invention also provides a method for preparing a ligand of formula (I) wherein n is 0, R^1 and R^3 are hydrogen, R^2 and R^4 are functional group-containing aryl groups and R^5, R^6, R^7 and R^8 are hydrogen,



(I)

comprising the steps of;

(a) Performing a benzoin condensation on a functionalised benzaldehyde to give a functionalised benzoin,

(b) reducing the functionalised benzoin to give a functionalised hydrobenzoin,

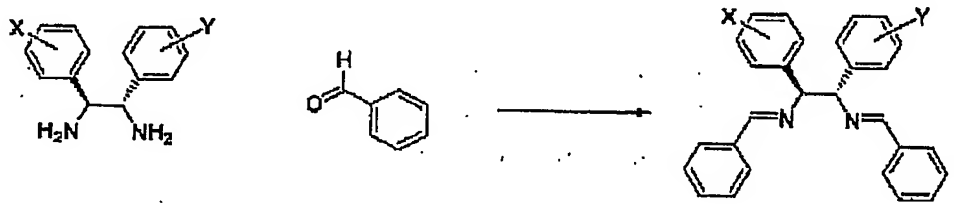
(c) transforming the functionalised hydrobenzoin into a functionalised 1,2-diarylamine, and

(d) reacting the functionalised 1,2-diarylamine with a solid support having a site capable of reacting with said functionalised 1,2-diarylamine.

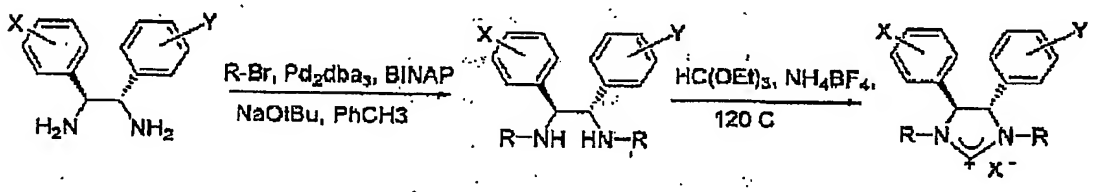
The functional group on the aryl group may be in the ortho, meta or para position. However, when the substituent is at the *meta*-position of the phenyl ring it minimizes the electronic effects on the amino group, which not only facilitates the synthesis of these diamines, but also benefits these diamines as ligands. Thus in a preferred embodiment the functionalised diamine is an enantiomerically pure 1,2-di-(*meta*-substituted phenyl)ethylenediamine. The synthesis of a 1,2-di-(*meta*-substituted phenyl)ethylenediamine begins, for example, with the *meta*-substituted benzaldehyde. By benzoin condensation, the corresponding benzoins, are obtained in over 90% yield. Reduction of the functionalised benzoins may be performed by methods know to those skilled in the art e.g. asymmetric reduction. Preferably the reduction is performed by an asymmetric hydrogen transfer hydrogenation using a chiral Ru catalyst. For example, in the presence of 0.1 mol% of RuCl[(R,R)-Tsdpen)(η^6-p-cymene), using a mixture of HCOOH-Et_3N (3.1:2.6) as hydrogen source, asymmetric transfer hydrogenation of the substituted benzoins affords the substituted (S,S)-hydrobenzoins, quantitatively with high diastereomeric (>95% de). Conversion of the functionalised hydroxy benzoin to the functionalised 1,2-diarylamine may be performed by methods known to those skilled in the art. Preferably the conversion is performed by (a) forming the diazide, and (b) converting the diazide into the diamine. This is preferably performed using the tosyl derivative of the functionalised hydroxybenzoin. Treatment of the (S,S)-hydrobenzoin with tosyl chloride (TsCl) in pyridine gives the corresponding 1,2-ditosyloxy derivatives, which may be used directly for next step without purification. By reacting the 1,2-ditosyloxy derivatives with sodium azide in DMF at 75-80°C for 8 h, the (R,R)-1,2-diazides, are obtained in good yield. Finally, the (R,R)-1,2-diazides may be reduced to substituted 1,2-(R,R)-diphenylethylenediamines in almost quantitative yield by $LiAlH_4$ in Et_2O.

As stated above, linker groups may be reacted with the ligands prior to reaction of the linker-modified ligand with the solid support. For example, 1,2-(R,R)-diphenylethylenediamines may be reacted with linking groups such a polyethylene glycol (PEG) to prepare soluble PEG modified 1,2-(R,R)-diphenylethylenediamines. This may be performed for example by protection of the benzyl-functionalised DPEN or TsDPEN with Boc, hydrogenolysis, reaction with polyethylene glycol, e.g. PEG 2000 as the monomethyl ether mesylate and removal of Boc. The polyethylene glycol monomethyl ether mesylate may be prepared from polyethylene glycol, e.g. PEG 2000 monomethyl ether by sulfonation with MsCl in the presence of base. To regenerate the PEG hydroxyl groups, the methyl ether may be e.g. hydrolysed using known methods.

It is possible to inter-convert the diamines of the present invention using known methods to provide the imine and cationic ligands. For example, reaction of the amine groups with aldehydes or ketones provides imines. An example of this reaction is depicted below;



More recently, methods have been developed for transformation of diamines into cationic precursors to carbenes (see for example Grubbs et al. *Org lett.*1999, vol 1, 953). An example of this reaction is depicted below;



The inter-conversion reactions may be performed upon the diamine ligand before or after reaction with the solid support.

The solid support materials to which the nitrogen-containing ligand having a functional group is covalently bonded, may be polymers, metal oxides or silica materials that have sites capable of reacting with said functional group. The metal oxides include silica, titania, zirconia or alumina, or mixtures of these. The polymers may be any that are insoluble in the solvent system used for performing the catalysed reaction and are stable under the reaction conditions. Preferably, where the reaction is performed in polar solvents, the polymer is a polystyrene or a polystyrene copolymer of suitable molecular weight, which may be further functionalised, e.g. with polyethyleneglycol or aminomethyl groups. By the term "silica materials" we mean organofunctional silica materials prepared, for example, by hydrolysis of organofunctional silanes, preferably in the presence of alkyl silicates and optionally other metal alkoxides.

The solid support materials have reactive sites capable of reaction with the functional group-containing ligand. These reactive sites may be selected from halide (Cl, Br, F, or I), hydroxyl, carbonyl, carboxyl, anhydride, carbene, methacryl, epoxide, vinyl, nitrile, mercapto, isocyanate, amine, imine, amide and imide.

In the case of metal oxides, the sites on the solid support that react with the functional group-containing ligand may be surface hydroxyl groups, which are present on the hydrated surfaces, or may be the result of surface functionalisation. Surface functionalisation of the oxides may be

carried our using a variety of organic compounds such as carboxylic acids, anhydrides, phosphates, or sulphonates or metal-organic compounds such as organic titanates, aluminates, zirconates or organofunctional silanes. Preferably surface functionalisation is performed using organofunctional silanes. Organofunctional silanes useful for the present invention include vinyltrimethoxy silane, vinyltriethoxysilane, dichlorodivinylsilane, 3-(aminopropyl)trimethoxysilane, 3-(aminopropyl)triethoxysilane, (3-(methacryloyloxy)-propyl]trimethoxysilane, [3-[tri(ethoxy/methoxy)silyl]propyl]urea, 3-(glycidoxypropyl)trimethoxysilane, 4-(triethoxysilyl)butyronitrile, 3-(Iodopropyl)trimethoxysilane, 3-(mercaptopropyl)-trimethoxysilane, 3-(triethoxysilyl)propionitrile, 4-(triethoxysilyl)butyronitrile , ((chloromethyl)-phenylethyl)trimethoxysilane, and ((chloromethyl)phenyl)trimethoxysilane and mixtures of these. Furthermore, in order to control the concentration of functional groups and/or prevent any undesirable side reaction of catalytically active metal complex with surface hydroxyl groups, it may be desirable to include with the organofunctional silane with a non-functionalised silane. Suitable non-functionalised silanes include alkyl silanes having 1 to 16 carbon atoms such as propyltrimethoxysilane, propyltriethoxysilane, butyltrimethoxysilane, hexylbutyltrichlorosilane, dodecyltrichlorosilane, octadecyltrimethoxysilane, octyltrimethoxysilane, octyltriethoxysilane and mixtures of these.

Polymers often may be prepared by addition or condensation reactions of suitable monomers that include at least a proportion of a monomer having a suitable reactive site capable of reaction with the functional group-containing ligand. Alternatively a reactive site may be grafted on or formed by a functional group inter-conversion reaction. By functional group inter-conversion we mean changing the reactive site on the polymer to enable reaction with the functional group-containing ligand. For example, if the functional group containing-ligand has a pendant hydroxyl group capable of reaction with the polymer having a reactive site, it may be desirable to chemically convert the reactive site on the polymer from, for example a cyano-group to a carboxyl group or, a carboxyl group to an acid-chloride group, to facilitate a reaction between said polymer and the ligand. Furthermore the polymer may have one or more reactive sites. The advantage of this feature is that the support may be tailored to react with different ligands.

The polymers should be insoluble and stable under the reaction conditions. Polystyrene polymers and polystyrene functionalised with PEG of suitable molecular weight are preferred. A polystyrene functionalised with PEG, having a bromine-atom reactive site is available commercially as Tentagel S-Br. For example a polymer-supported 1,2-(R,R)-diphenylethylenediamine may be prepared by reaction of a hydroxyl-functionalised 1,2-(R,R)-diphenylethylenediamine.

The silica materials are preferably those as described in the aforementioned PCT application GB02/00527, prepared by the co-hydrolysis of an alkyl silicate and an organofunctional silane. The alkyl silicates are preferably tetraalkylsilicates which have the general formula $Si(OR)_4$ in which each R may be the same or different and is an alkyl group or substituted alkyl group having between 1 and 4 carbon atoms. The organofunctional silanes may be halo or alkoxy organofunctional silanes according to the general formula;

$(Y)_aSi((Z)X)_b$ in which;

Y is a halogen or alkoxy group having 1 to 3 carbon atoms;

Z is an alkyl, aryl or alkyl-aryl group which optionally contains at least one heteroatom selected from oxygen, nitrogen, phosphorus or sulphur; and

X is a functional group selected from halide, hydroxyl, carbonyl, carboxyl, anhydride, carbene, methacryl, epoxide, vinyl, nitrile, mercapto, amine, imine, amide and imide;

a = 3 or 2, b = 1 or 2 and a + b = 4.

In the above formula, if Z contains an alkyl group it preferably has between 1 and 16 carbon atoms, is branched or linear and saturated or unsaturated. If Z contains an aryl group it is preferably a substituted or unsubstituted phenyl, phenoxy or anilide moiety. Where X is bound to an alkyl group it may be bound on either a primary, secondary or tertiary carbon.

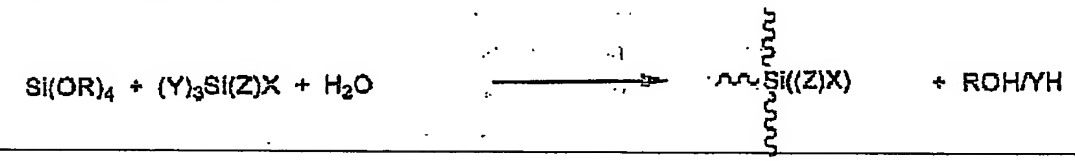
The organofunctional silane may be selected from those commercially available or if desired may be prepared by reaction of an organofunctional silane with a linker molecule that provides a functional group capable of reaction with a functional group-containing ligand. The linker molecule may be any that contains a functional group that is capable of reacting with the organofunctional silane and provides a suitable functional group in the resultant silica material capable of reacting with a functional group-containing ligand. Suitable linker molecules include C1-C10 alkyl, alkoxy, alkyl-aryl, aryl, phenoxy or anilide compounds containing functional groups selected from halide, hydroxyl, carbonyl, carboxyl, anhydride, carbene, methacryl, epoxide, vinyl, nitrile, mercapto, isocyanate, amine, imine, amide and imide. Advantages of preparing the organofunctional silane in this way are that new functional groups may be introduced in a way that is not generally possible in commercially available silanes, functional groups may be introduced at a greater distance from the silicon atom than is possible with currently available silanes, and such modification may provide organofunctional silanes that provide improvements in the properties of the resulting organofunctional silica, e.g. porosity.

Mixtures of organofunctional silanes having different functional groups may be used to prepare the organofunctional silica. In such mixtures 2 or more silanes may be present. This has the advantage that different diamines may be attached to different reactive sites on the organofunctional silica. Optionally, a silane not having a functional group capable of reaction with a functional group-containing diamine may be used in combination with an

organofunctional silane as described above to e.g. reduce the surface concentration of functional groups on the silica material and improve ligand attachment. Such non-functionalised silanes may also be used to improve other properties of the resulting silica material such as porosity or pore size. Silanes such as alkyl silanes can be used although other non-functionalised silanes may also be used. The molecular ratio of functionalised and non-functionalised silanes used may be any that provides a sufficient number of reactive sites for tethering the diamine containing a functional group to the resulting organofunctional silica to provide a useful level of catalytic activity in the final catalyst. Molecular ratios may be in the range 1:99 to 99:1 for any given pair of silanes, preferably 1:9 to 9:1.

Organofunctional silanes useful for preparing organofunctional silicas include vinyltrimethoxy silane, vinyltriethoxysilane, dichlorodivinylsilane, 3-(aminopropyl)trimethoxysilane, 3-(aminopropyl)triethoxysilane, [3-(methacryloyloxy)-propyl]trimethoxysilane, [3-[tri(ethoxy/methoxy)silyl]propyl]urea, 3-(glycidoxypropyl)trimethoxysilane, 4-(triethoxysilyl)butyronitrile, 3-(Iodopropyl)trimethoxysilane, 3-(mercaptopropyl)-trimethoxysilane, 3-(triethoxysilyl)propionitrile, 4-(triethoxysilyl)butyronitrile , ((chloromethyl)-phenylethyl)trimethoxysilane, and ((chloromethyl)phenyl)trimethoxysilane and mixtures of these. Non-functionalised silanes include alkyl silanes having 1 to 16 carbon atoms such as propyltrimethoxysilane, propyltriethoxysilane, butyltrimethoxysilane, hexylbutyltrichlorosilane, dodecyltrichlorosilane, octadecyltrimethoxysilane, octyltrimethoxysilane, octyltriethoxysilane and mixtures of these.

A method for preparing organofunctional silica by the co-hydrolysis of an alkyl silicate and an organofunctional silane is depicted below: The wavy-line represents the silicon atom on or within the resulting silica material.



In one embodiment, alkyl silicate and organofunctional silane are added to a mechanically stirred mixture of solvent and water. The alkyl silicate and organofunctional silane may be added together, sequentially in any order or in alternating portions. In an alternative embodiment the alkyl silicate, organofunctional silane and solvent are added to the mechanically stirred water and in yet a further embodiment the alkyl silicate and organofunctional silane without solvent are added to the mechanically stirred water. The alkyl silicate and organofunctional silane are added at a molecular ratio of greater than or equal to 1:1 (silicate:silane). Preferably the ratio of alkyl silicate to silane is between 1:1 and 99:1 and more preferably between 1:1 and 10:1. Typically the solvent, if used, is an alcohol but may be

any other solvent suitable for performing the co-hydrolysis reaction. For example, the solvent may be methanol, ethanol or propanol. Water is present in sufficient quantity to cause complete hydrolysis of the alkoxide moieties on the alkyl silicate and is generally added in large excess.

A template compound may be added to the hydrolysis mixture to influence the resulting pore structure and potentially the disposition of the organofunctionality within the pores of the resulting organofunctional silica. Depending upon the method used, the template may be added to for example, the solvent / water mixture, the alkyl silicate / organofunctional silane / solvent mixture or the alkyl silicate / organofunctional silane mixture. The templates function by becoming entrapped in the silica as it forms during the co-hydrolysis of the alkyl silicate and organofunctional silane. Once the co-hydrolysis is complete, the entrapped template may then be removed by, for example, solvent extraction to leave behind pores corresponding to the structure of the template molecule. Suitable solvents for solvent extraction include alcohols, e.g. ethanol. Template compounds may be used in the preparation of mico- and meso- porous silicas (where a micro-porous silica has an average pore width of less than 20 Å and a meso-porous silica has an average pore width of between 20 and 500 Å). Preferably the organofunctional silica is a meso-porous silica having an average pore width, as measured by BET porosimetry, of between 20 and 500 Å.

Template compounds include amines, quaternary ammonium salts and non-ionic poly(ethylene oxide)/(propylene oxide) surfactants such as amphilic block copolymers. Preferably the template molecule is an amine. Suitable amines are amines having 10 or more carbon atoms in the structure and preferably are C12 to C18 alkyl amines such as n-dodecylamine or n-octadecylamine or mixtures of these. The amount of template compound required will depend upon a number of factors including the amount of alkyl silicate used. In general the relative amounts of template molecule may vary in the range 1:10 to 50:1 and preferably in the range 1:1 to 10:1 parts by weight silicate:template compound.

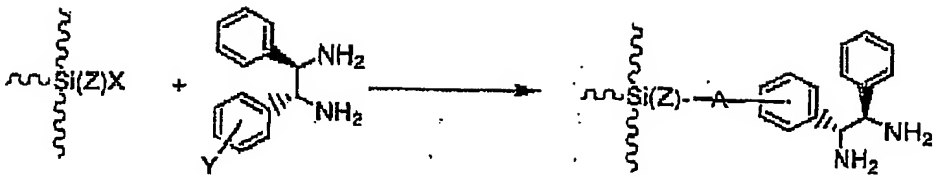
In addition to the template, a pore-enlarging additive may be included in the hydrolysis mixture. A known pore-enlarging additive is mesitylene (1,3,5-trimethylbenzene). Depending upon the method chosen for performing the co-hydrolysis reaction, the pore swelling additive may for example, be combined with the silicate and organofunctional silane or with the water or water/solvent mixture or may be added separately to the hydrolysis mixture. The amount of pore-enlarging additive that may be added will depend upon the properties of the additive, for example in the present invention 1-2 moles of mesitylene may be added per mole of alkyl silicate.

The co-hydrolysis reaction may be performed at room temperature or if desired at elevated temperature depending on the physical properties of the solvent chosen. For example the co-hydrolysis reaction may be carried out at between 10 – 50°C for periods between 1 and 36 hours. When the co-hydrolysis reaction is complete the organofunctional silica is recovered by, for example filtration and the template, if present, removed by solvent extraction. Solvent extraction may be effected for example by heating the re-suspended organofunctional silica in a suitable solvent such as ethanol. This may be repeated as necessary to remove all of the template prior to attachment of the functional group-containing diamine.

It may be desirable to perform a functional group inter-conversion, i.e. change the functional groups present on the organofunctional silica to provide a different functional group with which to react the functional group containing-ligand. For example, if the functional group containing-ligand has a pendant hydroxyl group capable of reaction with the organofunctional silica, it may be desirable to chemically convert the functional group on the silica from, for example a cyano-group to a carboxyl group or, a carboxyl group to an acid-chloride group, to facilitate a reaction between said silica and said ligand. Such conversions may also provide a means for providing functional groups on the organofunctional silica not practical as a result of the method used for its preparation. For example, isocyanate groups that would be unstable to the water used during the co-hydrolysis of alkyl silicate and organofunctional silane may be provided by inter-conversion of acid-chloride via a Curtis rearrangement. Alternatively, a chemical conversion may be performed to reduce the surface concentration of functional groups capable of reaction with the functional group-containing ligand by, for example, converting the functional groups to unreactive species such as hydrogen or alkyl groups.

Alternatively the organofunctional silica may be reacted with a linker molecule as hereinbefore described that provides a functional group capable of reaction with a functional group-containing ligand, to form a new organofunctional silica. This may be of particular use where chemical conversion of functional groups on the ligand is difficult.

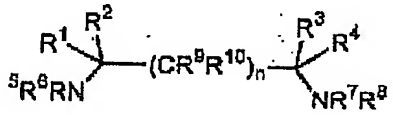
A reaction of a diamine containing a functional group with an organofunctional silica to provide a supported diamine is depicted below. Here Y represents the functional group on the diamine capable of reaction with the organofunctional silica and A represents the group resulting from the reaction of X and Y that bonds the diamine to the organofunctional silica. In an alternative embodiment, one of the diamine nitrogen atoms is protected with a removable group, e.g. a tosyl group;



The reaction may be achieved by any effective chemical reaction between the functional groups of the organofunctional silica and the nitrogen-containing ligand. Typical reactions include for example, esterification reactions, amidation reactions, addition reactions, substitution reactions, insertion reactions and carbon-carbon coupling reactions and may be performed by any method known to those skilled in the art. For example, esterification reactions may be performed between diamine and silica either having carboxyl and hydroxyl groups, anhydride and hydroxyl groups or acid-chloride and hydroxyl groups in the presence of suitable catalysts or reagents. Amidation reactions may be performed between ligand and silica either having carboxyl groups and primary or secondary amine groups or anhydride groups and primary or secondary amine, again in the presence of suitable catalysts or reagents.

In order to prepare an immobilised catalyst, a metal compound is reacted with the immobilised nitrogen-containing ligand.

Accordingly the invention further provides an immobilised catalyst comprising the reaction product of an immobilised nitrogen-containing ligand of formula (I)



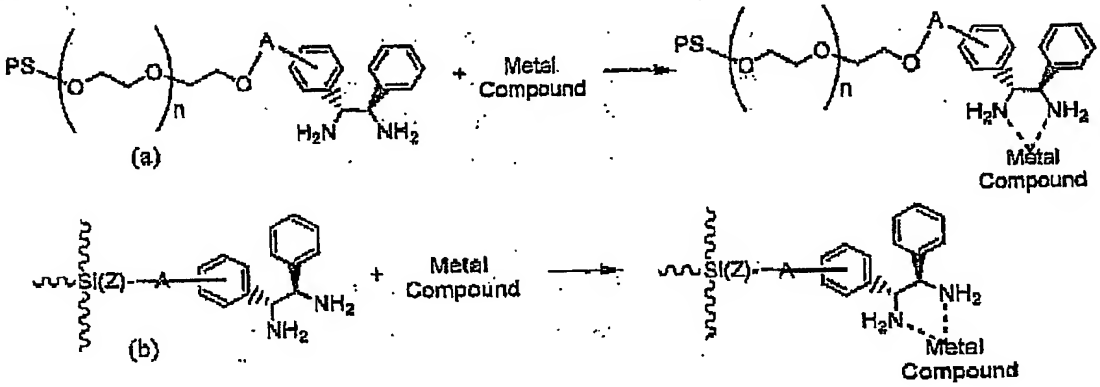
(I)

wherein R^5, R^6, R^7 and R^8 are independently hydrogen, a saturated or unsaturated C1-C10 alkyl group, an aryl group, a urethane group, a sulphonyl group or form an imine group, R^1, R^2, R^3, R^4, R^9 and R^{10} are independently hydrogen, a saturated or unsaturated C1-C10 alkyl group or an aryl group, n is 0-2, and at least one of R^1, R^2, R^3, R^4, R^9 and R^{10} is bound to a solid support, and a metal compound.

The metal compound is preferably a compound of Sc, Ti, Zr, Hf, V, Nb, Ta, Cr, Mo, W, Mn, Tc, Re, Fe, Ru, Co, Rh, Ir, Ni, Pd, Pt, Cu, Ag, Al, Ge, Sb or Sn. Preferably, for asymmetric hydrogenation reactions, the metal compound is a compound of Pd, Pt, Rh, Ir or Ru; preferably for hydrolytic kinetic resolution of epoxides the metal compound is a Co compound; preferably

for ring-opening reactions the metal compound is a Cr or an Al compound; and preferably for Heck reactions the metal compound is a Pd compound. The metal compound may be elemental metal, but is preferably a metal salt, e.g. halide, carboxylate, sulphonate or phosphonate, a metal alkyl or organometallic compound. For example rhodium may be reacted as a 1,5-cyclooctadiene complex and for manganese, palladium or cobalt the metal may be reacted as the di-acetate.

Reactions of a metal compound with a supported diamine to provide (a) a polymer-supported catalyst, and (b) a silica material-supported catalyst are depicted below, where A represents A represents the group resulting from the reaction of X and Y that bonds the diamine to the solid support;



The reaction between metal compound and immobilised nitrogen-containing ligand may be achieved by methods known to those skilled in the art and is preferably effected by reaction of a metal compound with the nitrogen-containing ligand in a suitable solvent. Such reactions include, for example, ligand substitution reactions and metal-insertion reactions. The metal may also, if desired, be subjected to steps of oxidation or reduction to provide the necessary catalytic activity. For example cobalt catalysts may be oxidised from Co(II) to Co(III) or rhodium catalysts may be reduced from Rh(III) to Rh(I).

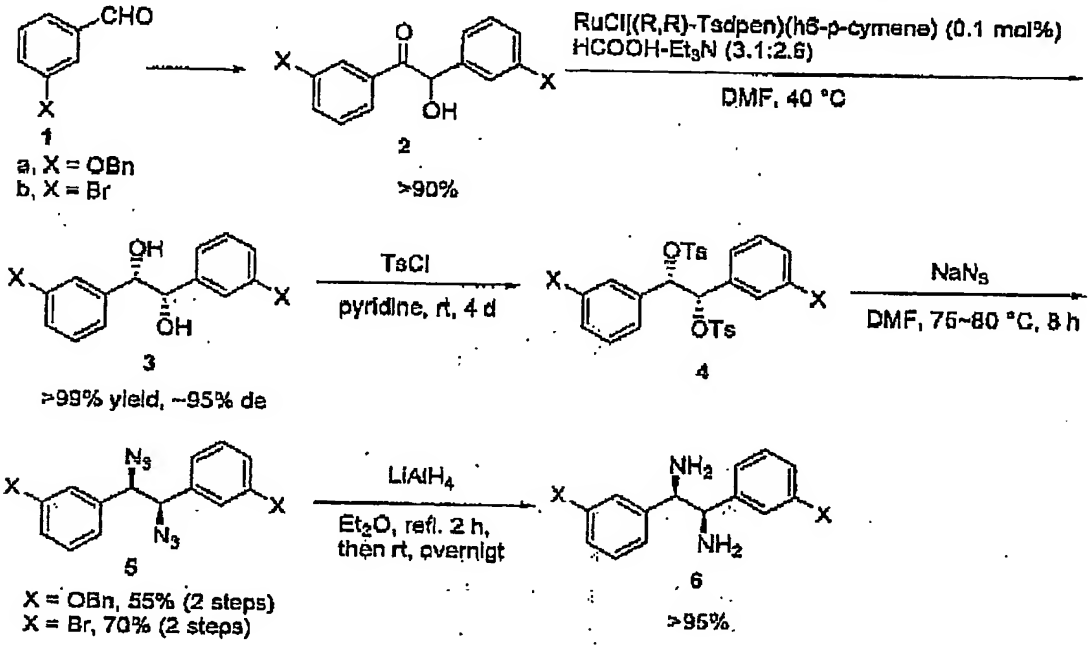
As stated above, preferably the supported nitrogen-containing ligands of the present invention are chiral ligands providing supported chiral catalysts. The supported chiral catalysts of the present invention may be applied to a large number of asymmetric reactions used to produce chiral products. Such reactions include hydrogenation reactions, including transfer hydrogenation reactions, dihydroxylation reactions, hydrolysis reactions, metathesis reactions, carbon-carbon bond formation reactions such as Heck or Suzuki reactions, hydroamination reactions, epoxidations, aziridinations, cycloadditions, hetero-Diels-Alder reactions, hetero-ene reactions, Claisen rearrangements, carbonyl reductions, sigmatropic rearrangements, additions of nucleophiles to π-bonds, addition of nucleophiles to carbonyl groups and ring-opening

reactions. Preferably the reactions are hydrogenation reactions, transfer hydrogenation reactions, hydrolysis reactions and carbon-carbon bond formation reactions. The advantages of the catalysts of the present invention are that they are readily separated from the reaction products and may be re-used if so desired.

The invention is illustrated by the following examples.

Example 1: Preparation of Diamine ligands

Functionalised 1,2-diarylamines were prepared according to the following scheme;



(a) Preparation of 3-Benzyloxybenzaldehyde (1a):

A suspension of 3-hydroxybenzaldehyde (36.64 g, 300 mmol), benzyl chloride (41.77 g, 330 mmol), anhydrous K_2CO_3 (49.76 g, 360 mmol) and NaI (1.0 g) in absolute EtOH (400 ml) was stirred and refluxed for 15 h. After cooling to room temperature, the salts were filtered off, and washed with CH_2Cl_2 (100 ml). The filtrate was evaporated under reduced pressure. The residue was dissolved in EtOAc (300 ml), washed with water (100 ml) and brine (100 ml), dried ($MgSO_4$), and evaporated under reduce pressure. The residue was recrystallized from MeOH to give the product (63.87 g, 96%) as colorless crystals. ^1H NMR ($CDCl_3$, δ): 9.97 (s, 1H), 7.22~7.48 (m, 9H), 5.12 (s, 2H).

(b) Preparation of 3,3'-Dibenzyloxybenzoin (2a):

A solution of 3-benzyloxybenzaldehyde (21.23 g, 100 mmol) and NaCN (2.50 g) in EtOH (100 ml) and water (40 ml) was refluxed for 8 h. Most of EtOH was removed under reduced

pressure. The residue was dissolved in EtOAc (200 ml), washed with water (2×100 ml) and brine (100 ml), dried ($MgSO_4$), and evaporated under reduced pressure. The residue was recrystallized from MeOH to give the product (19.52 g, 92%) as colorless crystals. ^1H NMR ($CDCl_3$, δ): 6.87~ 7.53 (m, 18 H), 5.84 (d, J = 3.8 Hz, 1H), 5.04 (s, 2H), 5.00 (s, 2H), 4.51 (d, J = 3.8 Hz, 1H).

(c) Preparation of 3,3'-Dibromobenzoin (2b):

A solution of 3-bromobenzaldehyde (18.50 g, 100 mmol) and NaCN (2.50 g) in EtOH (50 ml) and water (20 ml) was refluxed for 8 h. Most of EtOH was removed under reduced pressure. The residue was dissolved in EtOAc (200 ml), washed with water (2×100 ml) and brine (100 ml), dried ($MgSO_4$), and evaporated under reduced pressure. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc = 3:1) to give the product (17.22 g, 93%) as oils.

(d) Preparation of (S,S)- 3,3'-Dibenzyloxy-hydrobenzoin (3a):

A solution of dichloro(p-cymene)ruthenium (II) dimer (2.5 mg, 0.004 mmol) and (1R,2R)-N-p-toluenesulfonyl-1,2-diphenylethylenediamine (3.3 mg, 0.009 mmol) in DMF (5 ml) was stirred for 20min at room temperature, then 3,3'-dibenzyloxybenzoin (2a) (3.40 g, 8 mmol), formic acid (0.94 ml, 24.8 mmol) and Et_3N (2.90 ml, 20.8 mmol) were added. The mixture was degassed by four freeze-thaw cycles, and stirred at 40 °C for 24 h. The solvents were removed under reduced pressure. The residue was dissolved in EtOAc (20 ml), washed with water (2×10 ml) and brine (10 ml), dried ($MgSO_4$), and evaporated under reduced pressure. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc = 3:1) to give the product (3.18 g, 93%) as oils. ^1H NMR ($CDCl_3$, δ): 7.31~7.39 (m, 10H), 7.14 (t, J = 7.8 Hz, 2H)), 6.84 (ddd, J = 7.8, 2.5 and 1.3 Hz, 2H), 6.79 (dd, J = 2.5 and 1.3 Hz, 2H), 6.69 (dt, J = 7.8 and 1.3 Hz, 2H), 4.95 (s, 4H), 4.64 (s, 2H), 2.85 (s, 2H).

(e) Preparation of (S,S)- 3,3'-Dibromo-hydrobenzoin (3b):

A solution of dichloro(p-cymene)ruthenium (II) dimer (2.8 mg, 0.0045 mmol) and (1R,2R)-N-p-toluenesulfonyl-1,2-diphenylethylenediamine (3.7 mg, 0.01 mmol) in DMF (5 ml) was stirred for 20min at room temperature, then 3,3'-dibenzyloxybenzoin (2a) (3.33 g, 9 mmol), formic acid (1.05 ml, 27.9 mmol) and Et_3N (3.26 ml, 23.4 mmol) were added. The mixture was degassed by four freeze-thaw cycles, and stirred at 40 °C for 24 h. The solvents were removed under reduced pressure. The residue was dissolved in EtOAc (20 ml), washed with water (2×10 ml) and brine (10 ml), dried (MgSO4), and evaporated under reduced pressure. The residue was purified by flash chromatography (SiO2, hexane-EtOAc = 3:1) to give the product (3.06 g, 91%) as oils. ^1H NMR ($CDCl_3$, δ): 7.39 (d, J = 7.7 Hz, 2H), 7.37 (s, 2H), 7.10 (t, J = 7.7 Hz, 2H), 6.95 (d, J = 7.7 Hz, 2H), 4.62 (s, 2H), 2.96 (s, 2H).

(f) Preparation of (1S,2S)-1,2-Di(3-benzyloxyphenyl)-1,2-ditosyloxyethane (4a):
To a solution of (S,S)- 3,3'-dibenzyloxy-hydrobenzoin (3a) (10.00 g, 23.4 mmol) in pyridine (50 ml) was added portion-wise TsCl (10.73 g, 56.30 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 4 days, quenched with ice water (100 ml) and extracted with CH_2Cl_2 (3x50 ml). The combined organic layers were washed with 10% HCl (2x50 ml), saturated $NaHCO_3$ solution (50 ml) and brine (50 ml), dried ($MgSO_4$), and evaporated under reduced pressure to give the crude product, which was used directly in next step without further purification. ^1H NMR ($CDCl_3$, δ): 7.52 (d, J = 8.1 Hz, 4H), 7.30~7.42 (m, 10 H), 7.11 (d, J = 8.1 Hz, 4H), 6.97 (t, J = 7.8 Hz, 2H), 6.75 (dd, J = 7.8 and 2.4 Hz, 2H), 6.50 (d, J = 7.8 Hz, 2H), 5.53 (s, 2H), 4.82 (d, J = 12.7 Hz, 2H), 4.78 (d, J = 12.7 Hz, 2H), 2.33 (s, 6H). ^{13}C NMR ($CDCl_3$, δ): 158. 80, 144.85, 137.07, 135.41, 134.07, 129.78, 129.55, 128.41, 128.29, 120.64, 116.34, 113.95, 83.71, 70.30, 21.91.

(g) Preparation of (1S,2S)-1,2-Di(3-bromophenyl)-1,2-ditosyloxyethane (4b):
To a solution of (S,S)- 3,3'-dibromo-hydrobenzoin (3b) (8.56 g, 23.0 mmol) in pyridine (50 ml) was added portionwise TsCl (10.52 g, 55.2 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 4 days, quenched with ice water (100 ml) and extracted with CH_2Cl_2 (3x50 ml). The combined organic layers were washed with 10% HCl (2x50 ml), saturated $NaHCO_3$ solution (50 ml) and brine (50 ml), dried ($MgSO_4$), and evaporated under reduced pressure to give the crude product, which was used directly in next step without further purification. ^1H NMR ($CDCl_3$, δ): 7.50 (d, J = 8.3 Hz, 4H), 7.30 (ddd, J = 7.8, 1.8 and 1.0 Hz, 2H), 7.16 (d, J = 8.3 Hz, 4H), 6.98~7.02 (m, 4H), 6.91 (dd, J = 7.8 and 1.0 Hz, 2H), 5.49 (s, 2H), 2.39 (s, 6H). ^{13}C NMR ($CDCl_3$, δ): 146.39, 135.99, 133.46, 132.44, 130.73, 130.10, 130.01, 128.15, 128.49, 122.71, 82.46, 21.99.

(h) Preparation of (1R,2R)-1,2-Di(3-benzyloxyphenyl)ethane-1,2-diazide (5a):
A suspension of the crude (1S,2S)-1,2-Di(3-benzyloxyphenyl)-1,2-ditosyloxyethane (4a) (~23 mmol) and NaN_3 (3.90 g, 60 mmol) in DMF (100 ml) was stirred at 75 °C for 8 h. After cooling to room temperature, water (300 ml) was added, and extracted with EtOAc (4x50 ml). The combined organic layers were washed with water (2x100 ml),and brine (100 ml), dried ($MgSO_4$), and evaporated under reduced pressure. The resulting brown oil was purified by flash chromatography (SiO_2, hexane-EtOAc = 8:1) to give the product (6.13 g, 55%) as yellow oils. ^1H NMR ($CDCl_3$, δ): 7.38 (m, 10H), 7.14 (t, J = 7.7 Hz, 2H), 6.86 (dm, J = 7.7 Hz, 2H), 6.69 (m, 2H), 6.63 (d, J = 7.7 Hz, 2H), 4.96 (s, 4H), 4.55 (s, 2H).

(i) Preparation of (1R,2R)-1,2-Di(3-bromophenyl)ethane-1,2-diazide (5b):
This compound was prepared in the same way as compound (5a). Yield: 70%. ^1H NMR ($CDCl_3$, δ): 7.40 (dm, J = 7.8 Hz, 2H), 7.25 (dd, J = 1.8 and 1.3 Hz, 2H), 7.13 (t, J = 7.8 Hz, 2H), 6.96

(d, J = 7.8 Hz, 2H), 4.96 (s, 4H), 4.56 (s, 2H). ^{13}C NMR ($CDCl_3$, δ): 137.72, 132.07, 130.71, 130.14, 125.34, 122.76, 69.91.

(j) Preparation of (1R,2R)-1,2-Di(3-benzyloxyphenyl)ethane-1,2-diamine (6a):

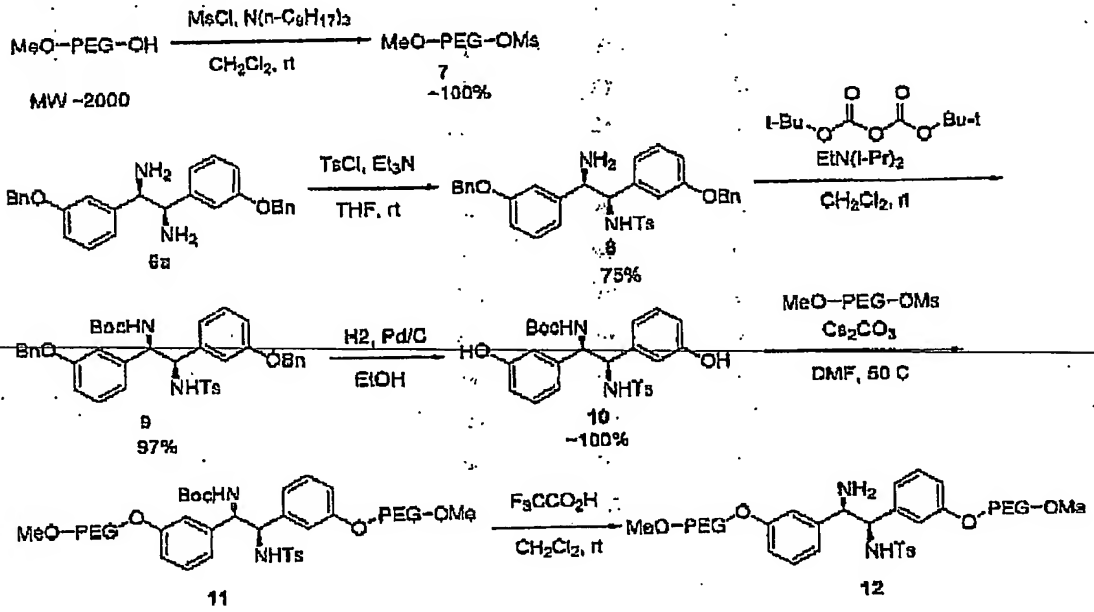
To a solution of (1R,2R)-1,2-di(3-benzyloxyphenyl)ethane-1,2-diazide (5a) (4.77 g, 10 mmol) in Et_2O was added portionwise $LiAlH_4$ (3.14 g, 83 mmol) at 0 °C. The resulting suspension was refluxed for 2 h, and then stirred at room temperature for overnight. Saturated Na_2SO_4 aqueous solution was carefully added to the reaction mixture. The solid was filtered off, and the filtrate was dried (Na_2SO_4) and evaporated under reduced pressure. The residue was triturated with hexane to give the product (4.08 g, 96%) as white solid. ^1H NMR ($CDCl_3$, δ): 7.29~7.43 (m, 10H), 7.19 (t, J = 7.8 Hz, 2H), 6.92 (dd, J = 2.4 and 1.8 Hz, 2H), 6.87 (br. d, J = 7.8 Hz, 2H), 6.84 (ddd, J = 7.8, 2.4 and 0.6 Hz, 2H), 5.02 (s, 4H), 4.05 (s, 2H), 1.64 (s, 4H). ^{13}C NMR ($CDCl_3$, δ): 159.19, 145.59, 137.47, 129.62, 128.93, 128.29, 127.86, 119.96, 114.00, 113.90, 70.41, 62.15.

(k) Preparation of (1R,2R)-1,2-Di(3-bromophenyl)ethane-1,2-diamine (6b):

This compound was prepared in the same way as compound 6a. Yield: 97%.

Example 2: Preparation of PEG-modified TsDPEN

Peg-modified TS DPEN was prepared according to the following scheme;



(a) Preparation of Polyethylene glycol 2000 monomethyl ether mesylate (7)

To a solution of polyethylene glycol 2000 monomethyl ether (20.00 g, 10 mmol) and tri-n-octylamine (13.10 ml, 30 mmol) in CH_2Cl_2 (50 ml) was added MsCl (1.55 ml, 20 mmol) at 0 °C.

The reaction mixture was stirred for 24 h at room temperature, and poured into Et_2O (1000 ml) with stirring. After stirring for 30 min at 0 °C, the precipitate was collected by filtration, washed with Et_2O (5×200 ml), and dried in vaccum to give the product (20.50 g) as white solid.

(b) Preparation of (R,R)-N-Tosyl-1,2-di(3-benzyloxyphenyl)ethane-1,2-diamine (8)

To a solution of (R,R)-1,2-di(3-benzyloxyphenyl)ethane-1,2-diamine (6a) (1.27 g, 3 mmol) and pyridine (2 ml) in THF (15 ml) was added dropwise a solution of TsCl (572 mg, 3 mmol) in THF (5 ml) at 0 °C. The reaction mixture was then allowed to warm to room temperature and stirred overnight. THF was removed under reduced pressure. The residue was dissolved in CH_2Cl_2 (30 ml), washed with saturated $NaHCO_3$ aqueous solution (10 ml), dried ($MgSO_4$), and evaporated under reduced pressure. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc = 1:4) to give the product (1.31 g, 75.3%) as white solid.

(c) Preparation of (R,R)-N-Boc-N'-tosyl-1,2-Di(3-benzyloxyphenyl)ethane-1,2-diamine (9)

To a solution of (R,R)-N-Tosyl-1,2-di(3-benzyloxyphenyl)ethane-1,2-diamine (8) (579 mg, 1.0 mmol) and N,N-diisopropylethylamine (0.26 ml, 1.5 mmol) in CH_2Cl_2 (5 ml) was added di-tert-butyl dicarbonate (240 mg, 1.1 mmol). The reaction mixture was stirred overnight at room temperature, washed with 1N HCl (5 ml) and brine (5 ml), dried ($MgSO_4$), and evaporated under reduced pressure. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc = 4:1) to give the product (649 mg, 95.6%) as white solid.

(d) Preparation of (R,R)-N-Boc-N'-tosyl-1,2-Di(3-hydroxyphenyl)ethane-1,2-diamine (10)

A suspension of (R,R)-N-Boc-N'-tosyl-1,2-di(3-benzyloxyphenyl)ethane-1,2-diamine (9) (600 mg, 0.88 mmol) and 10% Pd/C (20 mg) in EtOH (5 ml) was stirred for 2 h at room temperature under 10 bar of hydrogen. The reaction mixture was filtered through a pad of Celite, and the solvent was then removed under reduced pressure. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc = 1:1) to give the product (462 mg, 92.6%) as white foam.

(e) PEG-modified protected diamine (11)

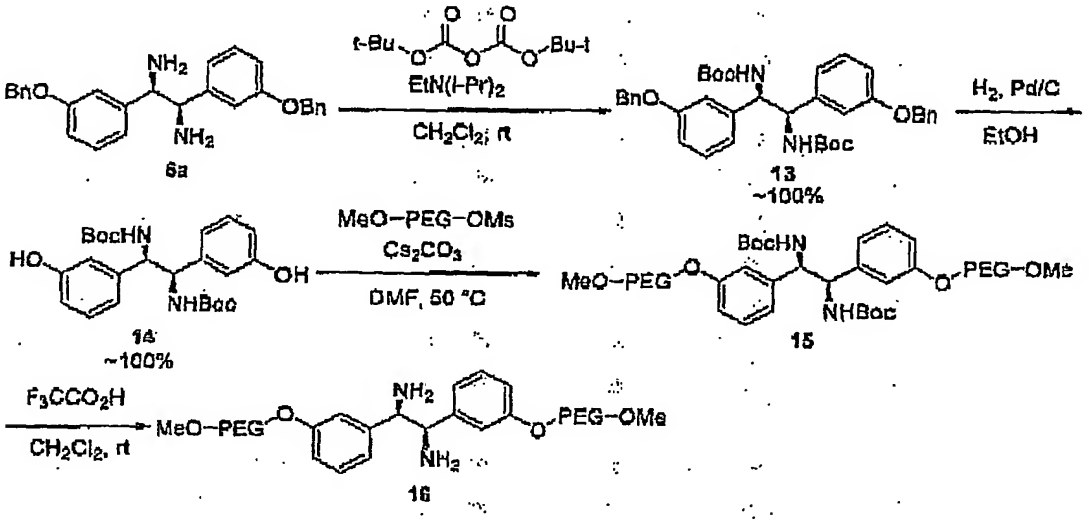
A suspension of (R,R)-N-Boc-N'-tosyl-1,2-di(3-hydroxyphenyl)ethane-1,2-diamine (10) (248 mg, 0.5 mmol), polyethylene glycol 2000 monomethyl ether mesylate (7) (2.00 g, 1.0 mmol) and Cs_2CO_3 (978 mg, 3.0 mmol) in DMF (10 ml) was stirred overnight at 50 °C. DMF was removed under reduced pressure; CH_2Cl_2 (10 ml) was then added. The insoluble salts were filtered off, and the filtrate was poured into Et_2O (150 ml) with stirring. After stirring for 30 min at 0 °C, the precipitate was collected by filtration, washed with Et_2O (5×20 ml), and dried in vaccum to give the product (2.15 g) as off-white solid.

(f) PEG-modified TsDPEN (12):

A solution of protected PEG-modified diamine (11) (2.0 g) in CH_2Cl_2 (5 ml) and CF_3CO_2H (5 ml) was stirred for 4 h at room temperature. The solvent was removed under reduced pressure. The residue was dissolved in CH_2Cl_2 (10 ml), and tri-n-octylamine (5 ml) was added. The mixture was stirred for 30 min at room temperature, and poured into Et_2O (150 ml) with stirring. After stirring for 30 min at 0 °C, the precipitate was collected by filtration, washed with Et_2O (5×20 ml), and dried in vaccum to give the product (1.93 g) as off-white solid.

Example 3: Preparation of PEG-modified DPEN

PEG-modified DPEN was prepared according to the following scheme;



(a) Preparation of (R,R)-N,N-Bis-Boc-1,2-di(3-benzyloxyphenyl)ethane-1,2-diamine (13):

To a solution of (R,R)-1,2-di(3-benzyloxyphenyl)ethane-1,2-diamine (6a) (1.32 g, 3.1 mmol) and N,N-diisopropylethylamine (1.21 ml, 7.0 mmol) in CH_2Cl_2 (10 ml) was added di-tert-butyl dicarbonate (1.42 g, 6.5 mmol). The reaction mixture was stirred overnight at room temperature, washed with 1N HCl (5 ml) and brine (5 ml), dried ($MgSO_4$), and evaporated under reduced pressure. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc = 4:1) to give the product (1.88 g, 97.3%) as white solid.

(b) Preparation of (R,R)-N,N-Bis-Boc-1,2-di(3-hydroxyphenyl)ethane-1,2-diamine (14):

A suspension of (R,R)-N,N-Bis-Boc-1,2-di(3-benzyloxyphenyl)ethane-1,2-diamine (13) (1.50 g, 2.4 mmol) and 10% Pd-C (50 mg) in EtOAc (10 ml) was stirred for 2 h at room temperature under 10 bar of hydrogen. The reaction mixture was filtered through a pad of Celite, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc = 1:1) to give the product (1.00 g, 93.7%) as white foam.

(c) PEG-modified protected diamine (15):

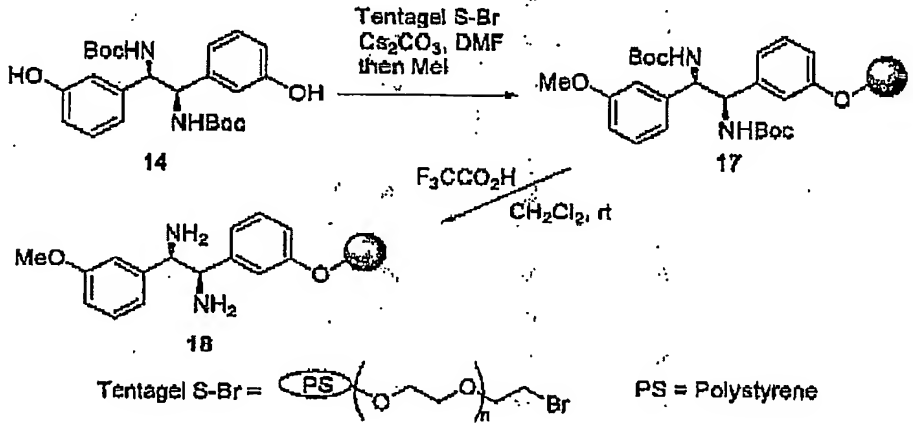
A suspension of (R,R)-N,N-Bis-Boc-1,2-di(3-hydroxyphenyl)ethane-1,2-diamine (14) (222 mg, 0.5 mmol), polyethylene glycol 2000 monomethyl ether masylate (55) (2.00 g, 1.0 mmol) and Cs_2CO_3 (978 mg, 3.0 mmol) in DMF (10 ml) was stirred overnight at 50 °C. DMF was removed under reduced pressure; CH_2Cl_2 (10 ml) was added. The insoluble salts were filtered off, and the filtrate was poured into Et_2O (150 ml) with stirring. After stirring for 30 min at 0 °C, the precipitate was collected by filtration, washed with Et_2O (5×20 ml), and dried in vacuum to give the product (2.10 g) as off-white solid.

(d) PEG-modified DPEN (16)

A solution of PEG-modified protected diamine (15) (2.0 g) in CH_2Cl_2 (5 ml) and CF_3CO_2H (5 ml) was stirred for 4 h at room temperature. Most of solvents were removed under reduced pressure. The residue was dissolved in CH_2Cl_2 (10 ml), and tri-n-octylamine (5 ml) was added. The mixture was stirred for 30 min at room temperature, and poured into Et_2O (150 ml) with stirring. After stirring for 30 min at 0 °C, the precipitate was collected by filtration, washed with Et_2O (5×20 ml), and dried in vacuum to give the product (1.95 g) as pale-yellow solid.

Example 4: Preparation of insoluble polymer-supported DPEN

Polymer supported DPEN was prepared according to the following scheme;



(a) Preparation of protected supported diamine (17):

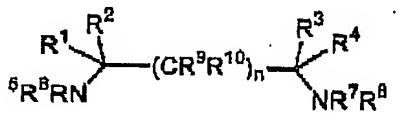
A suspension of (R,R)-N,N-Bis-Boc-1,2-di(3-hydroxyphenyl)ethane-1,2-diamine (14) (311 mg, 0.7 mmol), Tentagel S-Br (0.2~0.3 mmol/g, 2.00 g, ~0.5 mmol) and Cs_2CO_3 (978 mg, 3.0 mmol) in DMF (10 ml) was stirred 24 h at 70 °C. After cooling to room temperature, MeI (0.1 ml, 1.6 mmol) was added, and the suspension was stirred for another 16 h at 40 °C. After cooling to room temperature, the mixture was diluted with H_2O (20 ml). The solid was collected by filtration, washed with H_2O, MeOH, acetone and Et_2O, dried in vacuum to give polymer (17) (2.06 g) as yellow solid.

(b) Preparation of supported diamine (18):

A suspension of polymer (17) (2.06 g) in CH_2Cl_2 (5 ml) and CF_3CO_2H (5 ml) was stirred overnight at room temperature. The solid was filtered off, suspended in 5% Na_2CO_3 aqueous solution (10 ml), and stirred for 4 h at room temperature. The solid was collected by filtration, washed with H_2O, MeOH, acetone and Et_2O, dried in vacuum to give polymer (18) (1.99 g) as yellow solid.

Claims.

1. An immobilised nitrogen-containing ligand comprising the reaction product of a compound of formula (I)



(I)

wherein R^5, R^6, R^7 and R^8 are independently hydrogen, a saturated or unsaturated C1-C10 alkyl group, an aryl group, a urethane group, a sulphonyl group or form an imine group, R^1, R^2, R^3 ,R^4, R^9 and R^{10} are independently hydrogen, a saturated or unsaturated C1-C10 alkyl group or an aryl group, n is 0-2, and at least one of R^1, R^2, R^3 ,R^4, R^9 and R^{10} is functionalised with a functional group, and a solid support having a site capable of reacting with said functional group.

2. A ligand according to claim 1 wherein n is 0 or 1, R^1, R^3 and R^9 are hydrogen and at least one of R^2, R^4, and R^{10} is a functional group-containing aryl group.

3 A ligand according to claim 1 or claim 2 wherein R^5, R^6, R^7 and R^8 are hydrogen, sulphonyl or urethane groups.

4. A ligand according to claim 1 or claim 2 wherein NR^5R^8 and NR^7R^8 form imine (N=C) groups whereby R^6 and R^8 are omitted.

5. A ligand according to claim 1 or claim 2 wherein R^8 and R^6 form a ring linked by between 1 and 3 carbon atoms.

6. A ligand according to any one of claims 1 to 5 wherein the functional group that may be used to bond to the support is selected from halogen (Cl, Br, F or I), hydroxyl, alkoxy, carbonyl, carboxyl, anhydride, carbene, methacryl, epoxide, vinyl, nitrile, mercapto, amine, imine, amide and imide.

7. A ligand according to any one of claims 1 to 6 wherein the ligand is reacted with a linker molecule that provides a suitable functional group capable of reaction with the solid support.

8. A ligand according to claim 7 wherein the linker is polyethylene glycol.

9. A ligand according to any one of claims 1 to 8 wherein solid support material to which the nitrogen-containing ligand is covalently bonded is a polymer, metal oxide or silica material that has sites capable of reacting with said ligand, said sites selected from halide (Cl, Br, F, or I), hydroxyl, carbonyl, carboxyl, anhydride, carbene, methacryl, epoxide, vinyl, nitrile, mercapto, isocyanate, amine, imine, amide and imide.

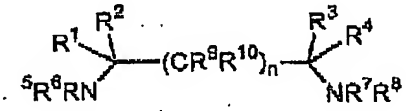
10. A ligand according to claim 9 wherein the solid support is silica, titania, zirconia, alumina or mixtures of these having reactive sites provided by organic compounds comprising carboxylic acids, anhydrides, phosphates, or sulphonates, or metal-organic compounds comprising organic titanates, aluminates, zirconates or organofunctional silanes.

11. A ligand according to claim 9 wherein the solid support is a reactive site-containing polystyrene or polystyrene copolymer.

12. A ligand according to claim 9 wherein the solid support is an organofunctional silica materials prepared by hydrolysis of organofunctional silanes.

13. A ligand according to claim 12 wherein the solid support is prepared by the co-hydrolysis of an organofunctional silane and an alkyl silicate and optionally other metal alkoxides.

14. A method for preparing a ligand of formula (I) wherein n is 0, R^1 and R^3 are hydrogen, R^2 and R^4 are functional group-containing aryl groups and R^5, R^6, R^7 and R^8 are hydrogen,



(I)

comprising the steps of ;

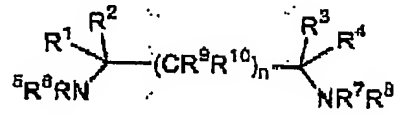
(a) Performing a benzoin condensation on a functionalised benzaldehyde to give a functionalised benzoin,

(b) reducing the functionalised benzoin to give a functionalised hydrobenzoin,

(c) transforming the functionalised hydrobenzoin into a functionalised 1,2-diarylamine, and

(d) reacting the functionalised 1,2-diarylamine with a solid support having a site capable of reacting with said functionalised 1,2-diarylamine.

15. An immobilised catalyst comprising the reaction product of an immobilised nitrogen-containing ligand of formula (I)



(I)

wherein R^6, R^8, R^7 and R^8 are independently hydrogen, a saturated or unsaturated C1-C10 alkyl group, an aryl group, a urethane group, a sulphonyl group or form an imine group, R^1, R^2, R^3 ,R^4, R^9 and R^{10} are independently hydrogen, a saturated or unsaturated C1-C10 alkyl group or an aryl group, n is 0-2, and at least one of R^1, R^2, R^3 ,R^4, R^9 and R^{10} is bound to a solid support, and a metal compound.

16. A catalyst according to claim 15 wherein the metal compound is a compound of Sc, Ti, Zr, Hf, V, Nb, Ta, Cr, Mo, W, Mn, Tc, Re, Fe, Ru, Co, Rh, Ir, Ni, Pd, Pt, Cu, Ag, Al, Ge, Sb or Sn.

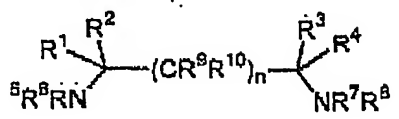
17. A catalyst according to claim 15 or claim 16 wherein the metal compound is a compound of Pd, Pt, Rh, Ir or Ru.

18. The use of an immobilised catalyst according to claim 15 for performing hydrogenation reactions, transfer hydrogenation reactions, dihydroxylation reactions, hydrolysis reactions, metathesis reactions, carbon-carbon bond formation reactions such as Heck or Suzuki reactions, hydroamination reactions, epoxidations, aziridinations, cycloadditions, hetero-Diels-Alder reactions, hetero-ene reactions, Claisen rearrangements, carbonyl reductions, sigmatropic rearrangements, additions of nucleophiles to π-bonds, addition of nucleophiles to carbonyl groups and ring-opening reactions.

19. The use of an immobilised catalyst according to claim 18 for performing hydrogenation reactions, transfer hydrogenation reactions, hydrolysis reactions and carbon-carbon bond formation reactions.

Abstract

An immobilised nitrogen-containing ligand is described comprising the reaction product of a compound of formula (I)



(I)

wherein R^5, R^6, R^7 and R^8 are independently hydrogen, a saturated or unsaturated C1-C10 alkyl group, an aryl group, a urethane group, a sulphonyl group or form an imine group, R^1, R^2, R^3 ,R^4, R^9 and R^{10} are independently hydrogen, a saturated or unsaturated C1-C10 alkyl group or an aryl group, n is 0-2, and at least one of R^1, R^2, R^3 ,R^4, R^9 and R^{10} is functionalised with a functional group, and a solid support having a site capable of reacting with said functional group. The nitrogen-containing ligand is useful for preparing immobilised catalysts for performing e.g. asymmetric catalysis.